

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
24 June 2004 (24.06.2004)

PCT

(10) International Publication Number
WO 2004/052213 A1

(51) International Patent Classification⁷: **A61B 17/00**

(21) International Application Number:
PCT/US2003/039253

(22) International Filing Date: 9 December 2003 (09.12.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/431,924 9 December 2002 (09.12.2002) US

(71) Applicant (for all designated States except US): NMT
MEDICAL, INC. [US/US]; 27 Wormwood Street,
Boston, MA 02210 (US).

Andrzej, J. [US/US]; 65 Greentree Lane, Apt. 48,
Weymouth, MA 02190 (US). DEVELLIAN, Carol, A.
[US/US]; 64 So. Main Street, Topsfield, MA 01983 (US).
PEAVEY, Todd, A. [US/US]; 90 Ellery Street, #32, Cam-
bridge, MA 02139 (US). WIDOMSKI, David [US/US];
One Sunset Drive, Wakefield, MA 01880 (US).

(74) Agents: DIENER, Michael et al.; Hale and Dorr LLP, 60
State Street, Boston, MA 02109 (US).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK,
MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT,
RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR,
TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

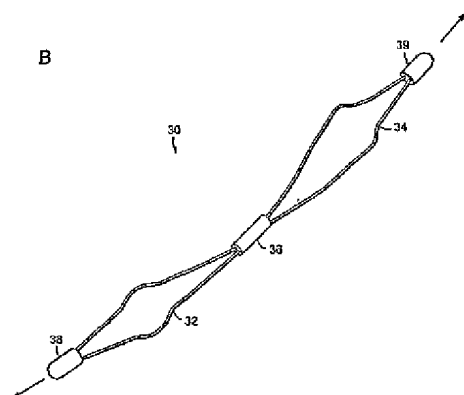
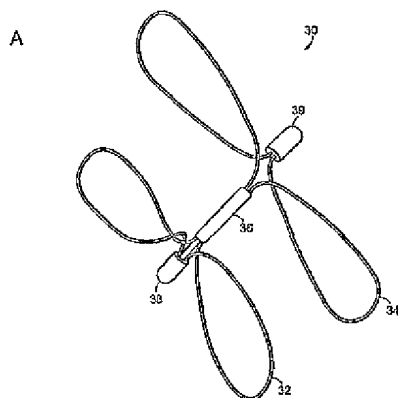
(84) Designated States (*regional*): ARIPO patent (BW, GH,
GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),

(72) Inventors; and

(75) Inventors/Applicants (for US only): CHANDUSZKO,

[Continued on next page]

(54) Title: SEPTAL CLOSURE DEVICES



(57) Abstract: A closure device for a patent foramen ovale (PFO) has proximal and distal occlusion members for applying compressive forces to tissue on opposite sides of septal defects to help close the defects. The devices are collapsible for delivery and deployment, and can be easily retrieved and redeployed or repositioned if needed.

WO 2004/052213 A1



Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

— before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

SEPTAL CLOSURE DEVICES

Cross-Reference to Related Application

This application claims priority from provisional serial no. 60/431,924, filed December 9, 2002, which is incorporated herein by reference.

5

Background of the Invention

A patent foramen ovale (PFO) as shown in FIG. 1 is a persistent, one-way, usually flap-like opening in the wall between the right atrium 10 and left atrium 12 of the heart. Since left atrial (LA) pressure is normally higher than right atrial (RA) pressure, the flap typically stays closed. Under certain conditions, however, RA pressure can exceed LA pressure, creating the possibility for right to left shunting that can allow blood clots to enter the systemic circulation.

In utero, the foramen ovale serves as a physiologic conduit for right-to-left shunting. After birth, with the establishment of pulmonary circulation, the increased left atrial blood flow and pressure results in functional closure of the foramen ovale. This closure is typically followed by anatomical closure of the two over-lapping layers of tissue, septum primum 14 and septum secundum 16. However, a PFO has been shown to persist in a significant minority of adults.

The presence of a PFO has no therapeutic consequence in otherwise healthy adults. But patients suffering a stroke or TIA in the presence of a PFO and without another cause of ischemic stroke are considered for prophylactic medical therapy to reduce the risk of a recurrent embolic event. These patients can be treated with oral anticoagulants, but such drugs have the potential for adverse side effects such as hemorrhaging, hematoma, and interactions with other drugs. In certain cases, such as when the use of anticoagulation drugs is contraindicated, surgery may be used to suture a PFO closed. Suturing a PFO requires attachment of septum secundum to septum primum with a stitch (continuous or interrupted), which is the common way a surgeon shuts the PFO under direct visualization.

Non-surgical closure of PFOs has become possible with umbrella devices and a variety of other similar mechanical closure designs developed initially for percutaneous closure of atrial septal defects (ASD). These devices allow patients to avoid the potential side effects often associated with anticoagulation therapies.

5 **Summary of Embodiments of the Invention**

Embodiments of the present invention are directed to devices for closing septal defects such as PFOs. The closure devices include proximal and distal occlusion members for applying compressive forces to tissue on opposite sides of septal defects to help close the defects. Material patches of a fabric or growth promoting matrix can optionally be applied to the occlusion members to cover the defect and promote tissue ingrowth to improve defect closure. The devices are collapsible for delivery and deployment, and can be easily retrieved and redeployed or repositioned if needed.

15 These and other features will become apparent from the following detailed description, wherein embodiments of the invention are shown and described by way of illustration. As will be realized, the invention is capable of other and different embodiments and its several details may be capable of modifications in various respects, all without departing from the invention. Accordingly, the drawings and
20 description are to be regarded as illustrative in nature and not in a restrictive or limiting sense.

Brief Description of the Drawings

FIG. 1 is a cross-sectional view of a portion of the heart illustrating a PFO;

FIGS. 2A and 2B are perspective views of a closure device in accordance with one or more embodiments of the invention in generally collapsed and expanded states, respectively;

FIGS. 3A – 3D are side views illustrating deployment of the closure device of FIGS. 2A and 2B in a PFO;

FIGS. 4A and 4B are perspective views of a closure device in expanded and collapsed states, respectively, in accordance with one or more further embodiments of the invention;

FIGS. 5A and 5B are perspective and side views, respectively, illustrating placement of the closure device of FIGS. 4A and 4B in a PFO; and

FIG. 6 is a side view of a closure device in accordance with one or more further embodiments of the invention.

Detailed Description

Various embodiments of the present invention are directed to methods and devices for closing septal defects such as PFOs. The devices apply compressive forces to compliant tissue on opposite sides of the defect to help close the defect.

FIGS. 2A-2B and 3A-3D generally illustrate a closure device or occluder in accordance with one or more embodiments of the invention. FIGS. 2A and 2B illustrate the device 20 in collapsed and expanded states, respectively. FIGS. 3A-3D illustrate a process of deploying the device 20. The device 20 is radially collapsible into a collapsed configuration (as shown in FIG. 2A) for delivery through a catheter and deployment. Upon deployment, it expands into a predefined expanded configuration (shown generally in FIG. 2B).

The device 20 includes an expandable distal occlusion member 22 and an expandable proximal occlusion member 24 connected to each other. The distal occlusion member 22 (which can be positioned on the left atrial side of a PFO) includes a framework having a central hub 26 and a plurality of outwardly extending elongated struts 28. The free ends of struts 28 can have small loops, ball tips, or

otherwise be rounded or configured to reduce trauma. The proximal occlusion member 24 (which can be placed on the right atrial side of the PFO) includes a plurality of wires in the form of loops 29, shown here as overlapping, when the device 20 is in an expanded state. As shown in FIGS. 2A and 2B, loops 29 each
5 extend from a central hub 26 to an end cap 27. The loop forms a plane that is approximately parallel to the tissue it is closing and applies a force that is generally perpendicular to the plane (see also FIG. 5A).

In accordance with some embodiments of the invention, material patches of a fabric or growth promoting matrix can optionally be applied to the occlusion
10 members 22, 24. When the device 20 is deployed, the patches can cover the defect and promote tissue ingrowth to improve defect closure. Numerous biocompatible materials can be used for the patches including, but not limited to, polyester fabrics (such as knitted or woven polyester fabrics), GORE-TEX® (ePTFE), and IVALON® (polyvinyl alcohol foam), naturally occurring tissue scaffolds (such as collagen or
15 acellular tissue matrices), polyurethane, bioresorbable tissue matrices, or electrospun fabric.

The wires forming the device are preferably made of a thermally responsive material having shape memory properties (e.g., nitinol, nitinol alloys, shape memory polymeric materials). The wires could be made of a bioresorbable materials if a
20 tissue scaffold is provided. Suitable shape memory materials can include a first, relatively pliable low temperature phase (mainly R-phase or martensite or both) and a second, relatively rigid high temperature phase (mainly austenite). Such material can, e.g., have a high temperature phase at about body temperature or, more preferably, at temperatures above about 70°F. As is generally known for such
25 materials, the device is collapsed in the R-phase or martensite phase, and then recovers a programmed shape when body heat causes the material in the device to transition to its austenitic phase. It should be understood that these are representative properties that can be varied.

In some respects, this device resembles a vena cava filter as shown in U.S.

Patent No. 4,425,908. A vena cava filter is designed to be inserted into a major vein to prevent a blood clot from entering the lungs, a different purpose from that described here.

FIGS. 3A-3D illustrate deployment of the device 20 for closing a PFO. The device 20 can be delivered to the septal defect in the collapsed state through a standard catheter 30. The catheter 30 is passed through the defect between septum primum 14 and septum secundum 16 as shown in FIG. 3A. The distal occlusion member 22 is then deployed as shown in FIG. 3B. The catheter 30 is retrieved, and the proximal occlusion member 24 is deployed on the proximal part of the defect as shown in FIGS. 3C and 3D. Once deployed, compressive forces are applied by the device 20 to the tissue, causing septum secundum 16 to be drawn toward septum primum 14. A tissue scaffold, if provided, would cause tissue to grow around the scaffold. The device 20 remains in place while the defect can heal to close the hole.

As indicated in FIG. 3D, the struts can just contact tissue at their ends, while the loops generally contact tissue over more of the length of the loops. If desired, the device 20 can be easily retrieved and redeployed or repositioned. The device 20 can be fully or partially pulled back into the delivery sheath from the defect by pulling on end cap 27, which serves as the proximal attachment point of the occluder for use with a recovery type catheter. The device can then be removed completely from the body or redeployed.

Benefits of the device 20 include high fatigue resistance, ability to be used with small diameter delivery sheaths, reduced metal mass, ease of manufacturing, reduced cost, and overall design simplicity.

FIGS. 4A and 4B generally illustrate a closure device or occluder 30 in accordance with one or more further embodiments of the present invention. FIG. 4A illustrates the device 30 in an expanded state when deployed, and FIG. 4B illustrates the device 30 in a generally collapsed state for delivery through a catheter.

The device 30 includes a distal occlusion member 32 (which can be positioned on the left atrial side of a PFO) and a proximal occlusion member 34 (which can be placed on the right atrial side of the PFO). When deployed, the occlusion members 32, 34 apply compressive forces to both sides of a defect, sandwiching the compliant tunnel tissue closed.

Each occlusion member 32, 34 in device 30 includes two collapsible propeller shaped wire petal members. The petals of the two occlusion members are joined by a connecting member 36, which extends into the tunnel defect when the device 30 is deployed. The loops that make up the propeller are shown extending from the central member 36 to end caps 38 and 39. These end caps, like the ones in the other embodiments, can be in a line with the connecting member 36 and can be perpendicular to septum primum and septum secundum if deployed to close a PFO; or they could be not in a line and/or could be skewed relative to a line perpendicular to septum primum and septum secundum if deployed to close a PFO

The petals collapse when the device 30 is pulled at opposite ends as shown in FIG. 4B. This collapsibility allows the device 30 to be elongated for loading into a delivery catheter. Device delivery can be achieved percutaneously by advancing the delivery catheter through the PFO defect. The device 30 can then be deployed. The device can be placed as illustrated, e.g., in FIGS. 5A-5B, with the petals generally oriented in-line with the defect. As shown, a plane defined by a loop is generally parallel to each septum and substantially perpendicular to the force applied by the loop. In FIG. 5A, the left atrial petals are illustrated generally in dashed lines and can be in the same circumferential location.

The device is preferably made from a material having shape memory properties such as Nitinol. This thermally responsive material allows the device petals to attain their desired deployed state geometry once released from the delivery catheter. The petals can be suitably sized to ensure that the device applies sufficient force to achieve defect closure.

The device 30 can close a PFO by applying compressive forces to the compliant flaps of the PFO. In accordance with some embodiments, to further promote hole closure, a fabric or a growth promoting matrix, which may include growth factors or other pharmacological agents or cells, can optionally be added to the petals to promote tissue growth over the device to plug the hole.

The petal design of the device provides wide surface contact with cardiac tissue on both the left and right atrial sides of the PFO defect. Substantial surface area contact by the petals enables generally evenly distributed pressure to be applied to close the PFO. The relatively simple structure of the device 30 allows use of an implant having a reduced metal mass. The device design also facilitates easy manufacture. The device can be made, e.g., by crimping, welding, or otherwise joining the device together in the petal geometry and then annealing.

While the FIG. 4 device 30 has two petals on each of the proximal and distal sides of the device, it should be understood that any number of petals can be used. For example, FIG. 6 illustrates a device 40 having more than two petals on each of the proximal and distal sides of the device. As shown in FIG. 6, the loops on one side are not necessarily at the same circumferential location as loops on the other side.

Having described various embodiments of the present invention, it should be apparent that modifications can be made without departing from the spirit and scope of the invention. The device is described for use with a PFO, but could be used for an atrial septal defect or a ventricular septal defect, in which case the device would typically have a tissue scaffold or other fabric.

What is claimed:

Claims

1. An apparatus comprising:

a patent foramen ovale (PFO) closure device having a deployed configuration for providing compressive force to septum primum and septum secundum and

5 including:

a central body for extending through the PFO,

a first end cap, and

first and second loops on one side of the PFO, each of the first and second loops extending from the central body to the first end cap, each of the first and second loops defining a plane substantially parallel to septum primum and septum secundum such that the first and second loops apply a force, perpendicular to the plane, to one of septum primum and septum secundum.

10

2. The apparatus of claim 1, further comprising, on the other side of the PFO, a plurality of struts extending radially from the central body and having ends for contacting one of septum primum and septum secundum.

15

3. The apparatus of claim 1, further comprising, on the other side of the PFO, a second end cap, and third and fourth loops on one side of the PFO, each of the third and fourth loops extending from the central body to the first end cap and second end cap, each of the third and fourth loops defining a plane substantially parallel to septum primum and septum secundum such that the first and second loops apply a force, perpendicular to the plane, to one of septum primum and septum secundum.

20

4. The apparatus of claim 3, where there are three or more loops on each side of the PFO.
5. The apparatus of claim 3, wherein the central body and the first and second end caps are oriented in a line substantially perpendicular to septum primum and septum secundum.
6. The apparatus of claim 1, wherein the device has a collapsed configuration for delivery through a catheter.
7. The apparatus of claim 6, wherein the device includes nitinol.
8. The apparatus of claim 6, wherein the device includes a shape memory polymeric material.
9. The apparatus of claim 6, wherein the device is made from a shape memory material with properties such that the device, when delivered into a body, has a phase transition and assumes the deployed configuration.
10. The apparatus of claim 1, wherein the device is retrievable, redeployable, and repositionable.
11. The apparatus of claim 1, further comprising a material over the first and second loops for promoting tissue ingrowth.
12. The apparatus of claim 11, wherein the loops are made of a bioresorbable material.
13. The apparatus of claim 3, further comprising a material over the first and second loops for promoting tissue ingrowth.

14. A method comprising delivering the PFO closure device of claim 1 through a catheter to a PFO.
15. A method comprising delivering the PFO closure device of claim 2 through a catheter to a PFO.
- 5 16. A method comprising delivering the PFO closure device of claim 3 through a catheter to a PFO.
17. A method comprising delivering the PFO closure device of claim 4 through a catheter to a PFO.
18. A method comprising delivering the PFO closure device of claim 1 through a
10 catheter to a PFO, wherein the device includes a shape memory material.
19. A method comprising delivering the PFO closure device of claim 10 through a catheter to a PFO.
20. A method comprising delivering the PFO closure device of claim 11 through a catheter to a PFO.
- 15 21. A method comprising delivering the PFO closure device of claim 12 through a catheter to a PFO.
22. A method comprising delivering the PFO closure device of claim 12 through a catheter to a PFO, and drawing the device back into the catheter..
- 20 23. An apparatus comprising:

a septal defect closure device having a deployed configuration for providing compressive force to septum primum and septum secundum and including:

a central body for extending through the defect,

a first end cap, and

5 first and second loops on one side of the defect, each of the first and second loops extending from the central body to the first end cap, each of the first and second loops defining a plane substantially parallel to septum primum and septum secundum such that the first and second loops apply a force, perpendicular to the plane, to one of septum primum and septum secundum.

10 24. A method comprising delivering the closure device of claim 23 through a catheter to a septal defect.

1/10

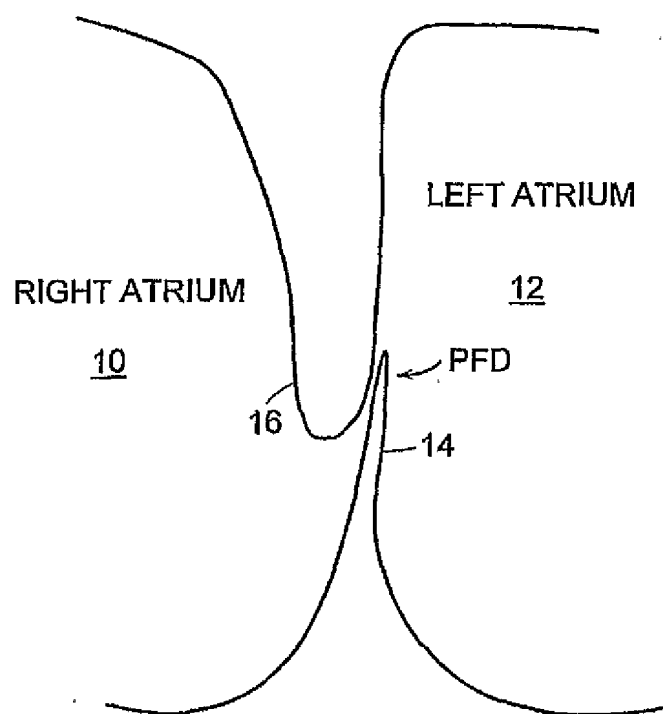


FIG. 1

2/10

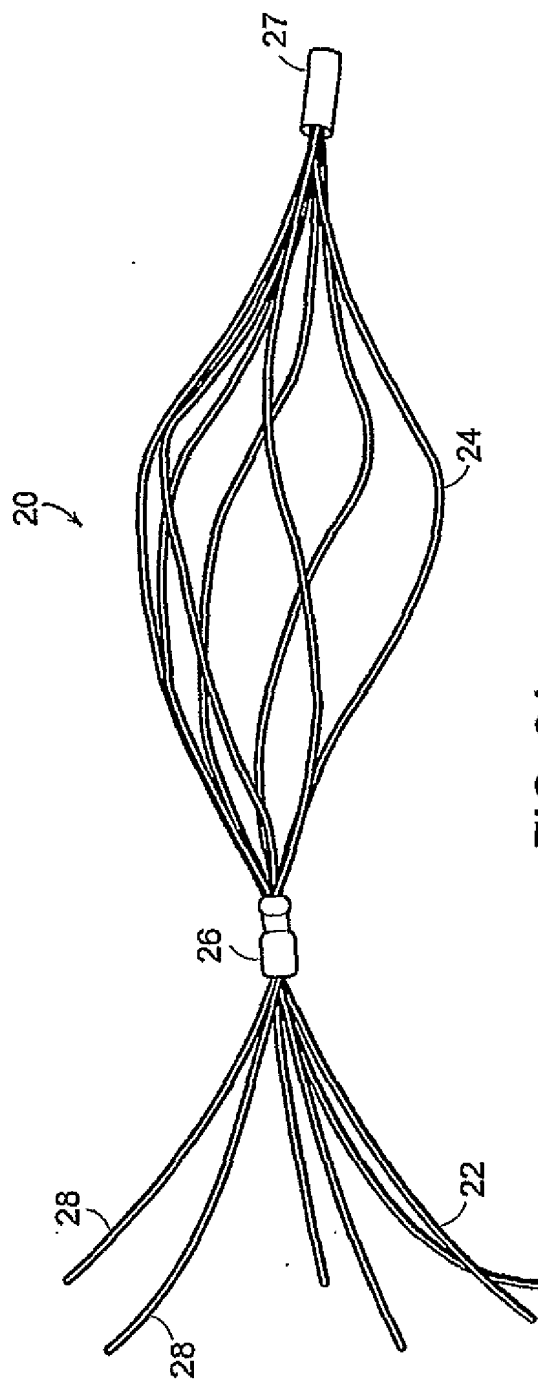


FIG. 2A

3/10

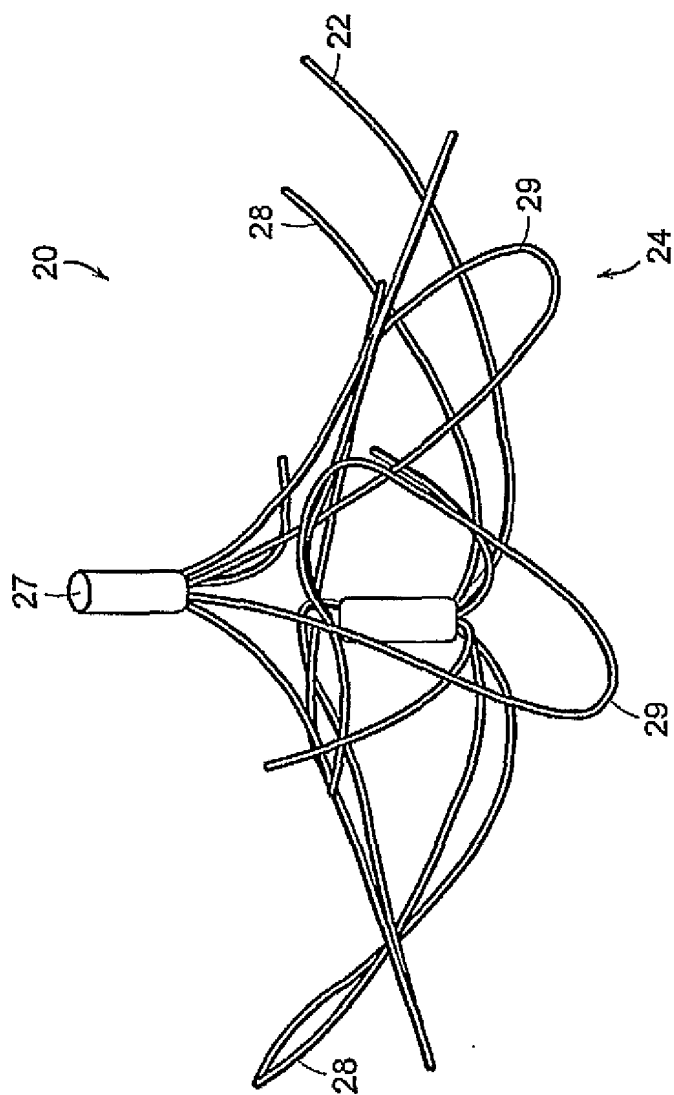


FIG. 2B

4/10

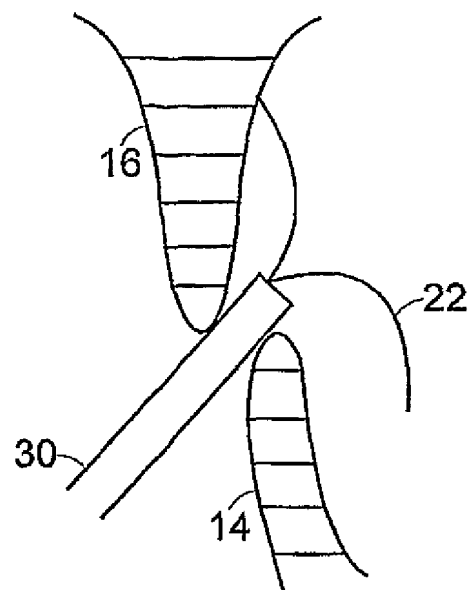


FIG. 3A

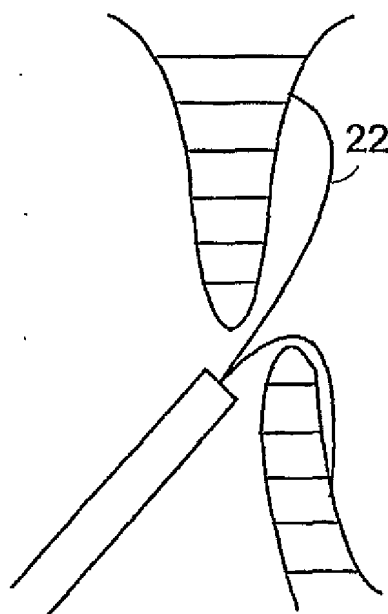


FIG. 3B

SUBSTITUTE SHEET (RULE 26)

5/10

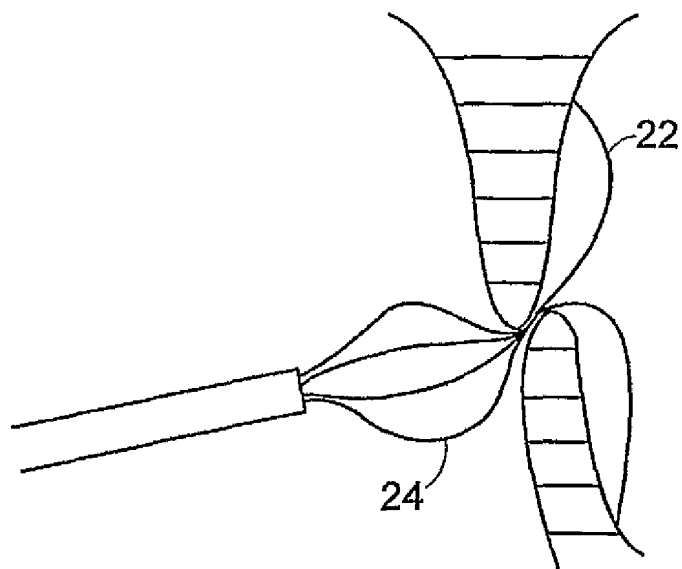


FIG. 3C

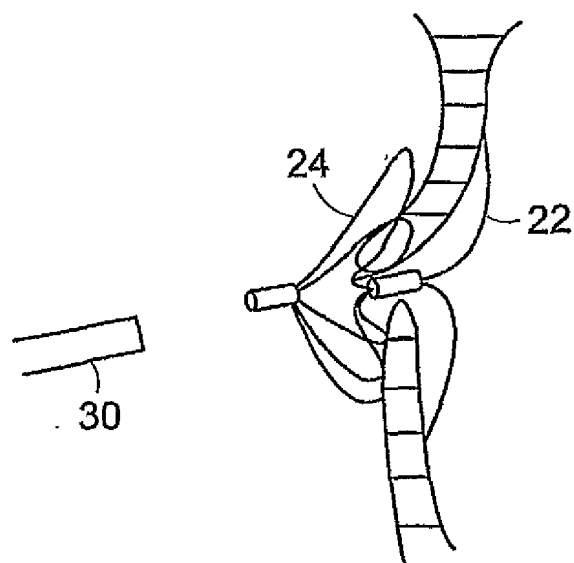


FIG. 3D

6/10

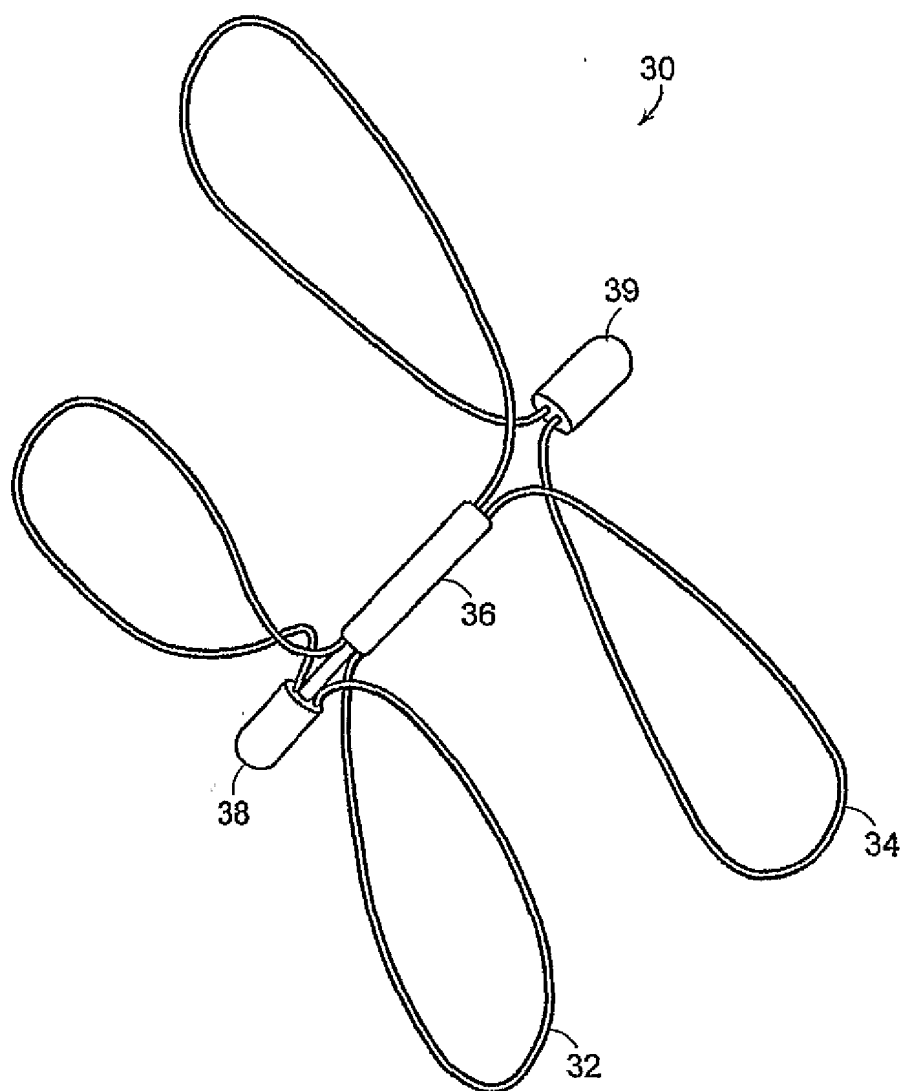


FIG. 4A

7/10

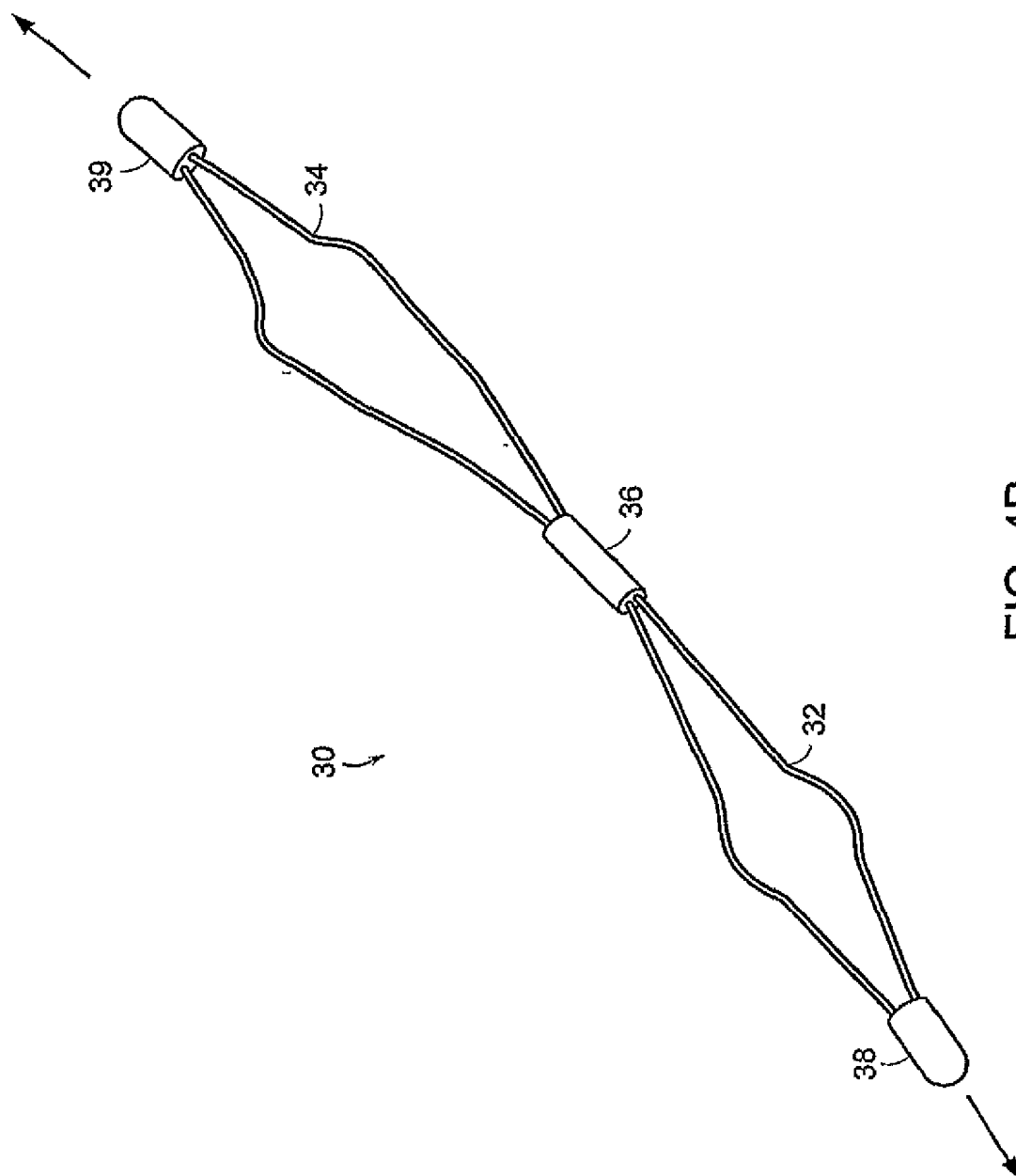
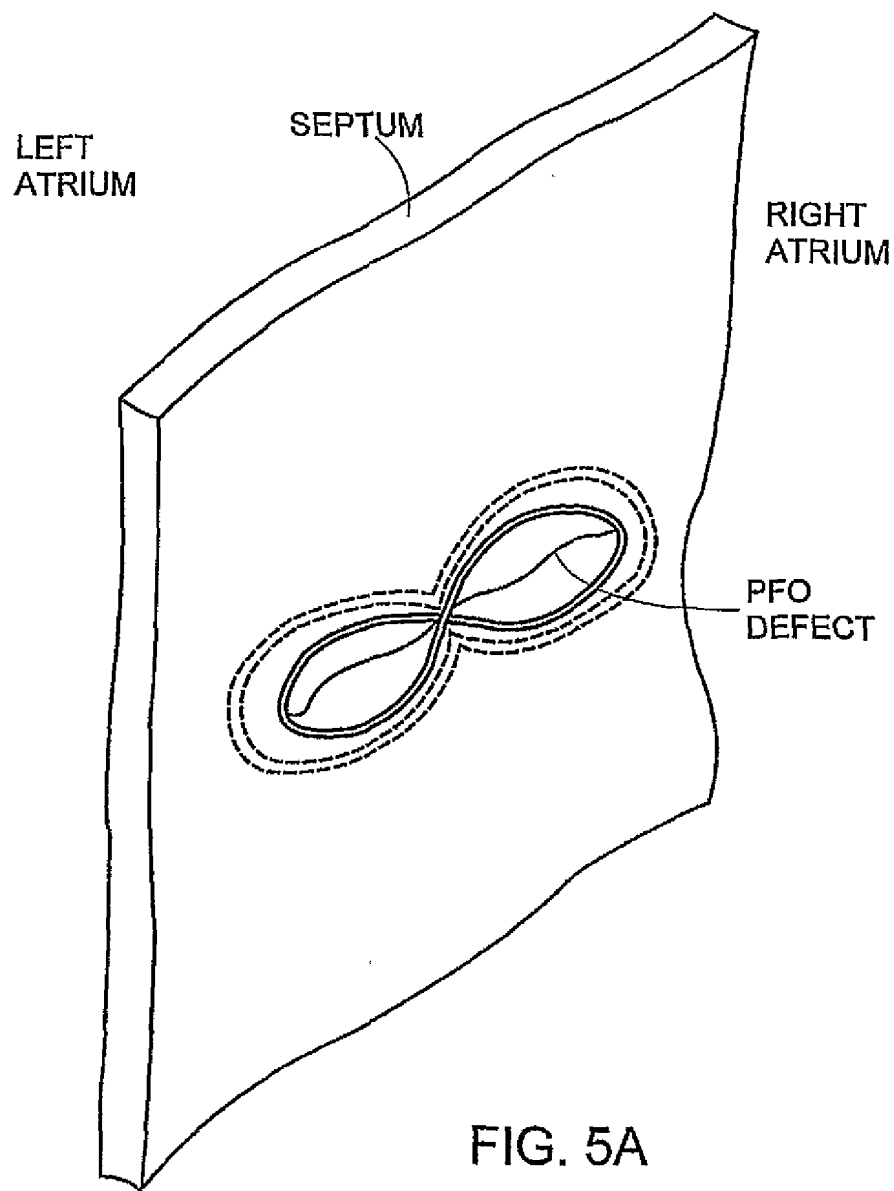


FIG. 4B

8/10



9/10

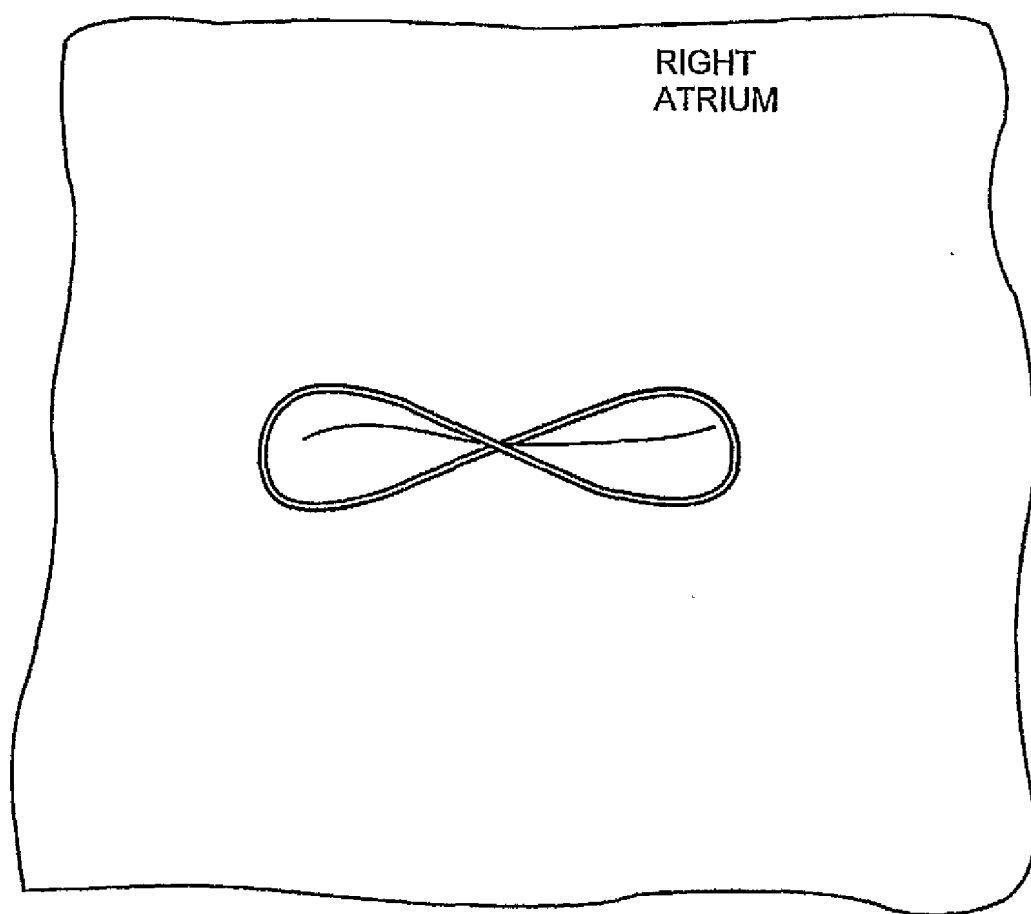


FIG. 5B

10/10

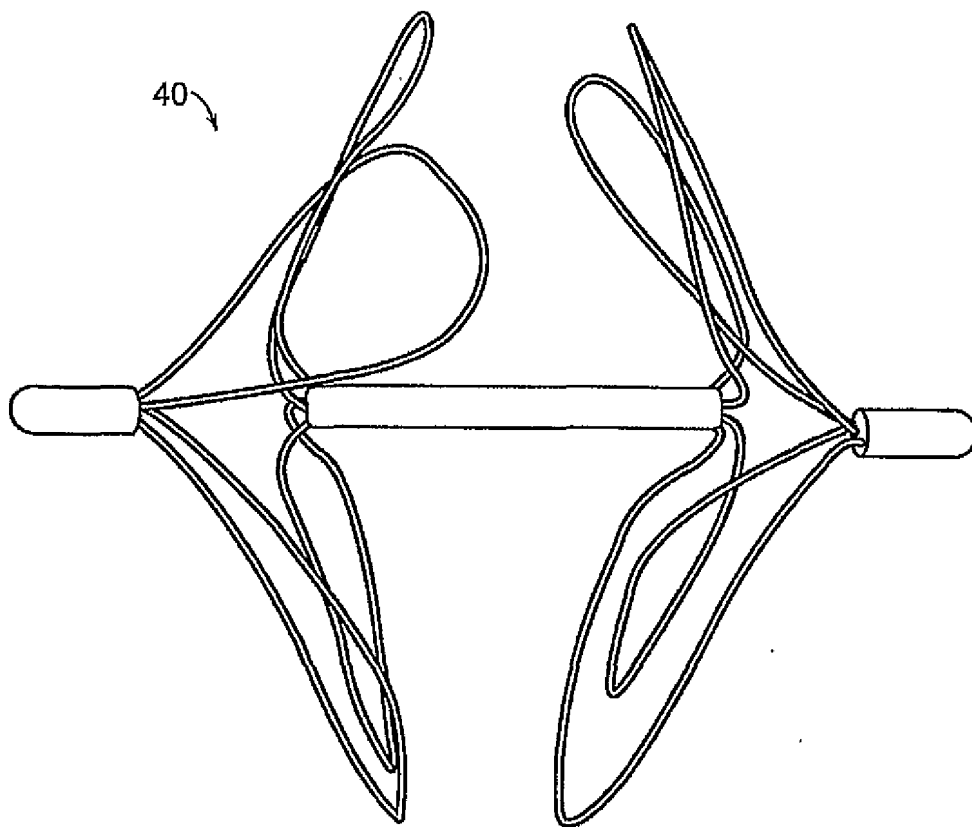


FIG. 6

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 03/39253

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61B17/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 944 738 A (AMPLATZ) 31 August 1999 (1999-08-31)	1,3-7, 9-11,13, 23 2
Y		
X	US 6 117 159 A (HUEBSCH) 12 September 2000 (2000-09-12) column 3, line 55 - column 4, line 33; figures 3,4 column 7, line 37 - line 67	1,3-13, 23
Y	EP 1 013 227 A (NISSHO) 28 June 2000 (2000-06-28) figure 1	2
A	US 2002/129819 A1 (FELDMAN) 19 September 2002 (2002-09-19) the whole document	8
	-/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

Z document member of the same patent family

Date of the actual completion of the international search

13 April 2004

Date of mailing of the international search report

19/04/2004

Name and mailing address of the ISA
European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Barton, S

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 03/39253

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 355 052 B1 (NEUSS) 12 March 2002 (2002-03-12) column 6, paragraph 3; figures 1-3 -----	1, 3-11, 13, 23
X	US 6 488 706 B1 (SOLYMAR) 3 December 2002 (2002-12-03) figures 11-15 -----	1
X	WO 01/49185 A (PFM) 12 July 2001 (2001-07-12) figures 8, 9, 13 -----	1, 3-7, 9-11, 13, 23

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 03/39253

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 14-22
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 03/39253

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5944738	A	31-08-1999	AU 737934 B2	06-09-2001
			AU 1074899 A	23-08-1999
			CA 2319521 A1	12-08-1999
			CN 1102373 B	05-03-2003
			EA 2106 B1	24-12-2001
			EP 1052944 A1	22-11-2000
			HK 1032892 A1	13-06-2003
			JP 2002502625 T	29-01-2002
			WO 9939646 A1	12-08-1999
US 6117159	A	12-09-2000	US 5853422 A	29-12-1998
			US 6312446 B1	06-11-2001
			US 6024756 A	15-02-2000
EP 1013227	A	28-06-2000	JP 2000185048 A	04-07-2000
			EP 1013227 A2	28-06-2000
			US 6342064 B1	29-01-2002
US 2002129819	A1	19-09-2002	WO 02060498 A1	08-08-2002
US 6355052	B1	12-03-2002	DE 19604817 A1	14-08-1997
			WO 9728744 A1	14-08-1997
			EP 0888083 A1	07-01-1999
			JP 2000505668 T	16-05-2000
US 6488706	B1	03-12-2002	SE 510577 C2	07-06-1999
			AU 2798497 A	26-11-1997
			EP 0959777 A1	01-12-1999
			JP 2001511658 T	14-08-2001
			RU 2190359 C2	10-10-2002
			SE 9601752 A	09-11-1997
			WO 9741779 A1	13-11-1997
			US 2003149463 A1	07-08-2003
WO 0149185	A	12-07-2001	DE 10000137 A1	12-07-2001
			AU 2512901 A	16-07-2001
			WO 0149185 A1	12-07-2001
			EP 1246570 A1	09-10-2002
			US 2003171774 A1	11-09-2003